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Effects of rhBNP after PCI on non-invasive hemodynamic in acute myocardial infarction patients with left heart failure

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ABSTRACT

Objective: To investigate the effects of exogenous recombinant human brain natriuretic peptide (rhBNP) after primary percutaneous coronary intervention (PCI) on non-invasive hemodynamic in acute myocardial infarction patients with left ventricular failure.

Methods: A number of 96 acute myocardial infarction patients accompanied with heart failure after PCI hospitalized in the People's Hospital of Sanya during February 2012 to October 2015 were selected. They were randomly divided into the therapy group (n = 50) and control group (n = 46). On the basis of routine treatment, patients in the therapy group were treated with intravenous rhBNP (1.5 μg/kg was intravenous injection with uniform speed of 3 min, followed by continuous infusion 0.007 5 μg/kg·min for 72 h), while the control group received conventional treatment. BioZ-2011 non-invasive hemodynamic real-time monitoring system was used to monitor the hemodynamic parameters changes and the leaves of plasma pro-BNP, serum creatinine, serum potassium, serum sodium and urine volume of each group before and after treating for 30 min, 1 h, 3 h, 6 h, 12 h, 24 h, 48 h, 72 h.

Results: Patients in the therapy group showed no effect on heart rate, while after 30 min of intravenous injection of rhBNP, CO, CI, SV, and SI increased significantly and LVET and TFC reduced at the same time, which had certain effect on blood pressure (SBP/DBP). Compared with the control group, the therapy group showed a faster and more effective improvement on hemodynamics.

Conclusions: Acute myocardial infarction patients complicated with left heart failure after primary PCI can significantly improve hemodynamics by treating with rhBNP.

1. Introduction

Acute myocardial infarction (AMI) has been a disease threatening human health seriously, because infarction can cause necrosis of a large number of myocardial cells, stunned myocardium, apoptosis, severe deletion of myocardial cells, which can lead to heart dysfunction directly, initiate neuroendocrine-activated myocardial remodeling of cell and heart failure. Percutaneous coronary intervention (PCI) is an effective method to save ischemic myocardium and protect heart function, which decreases the mortality rate of AMI patients distinctly. However, heart failure still occurs in AMI patients after they have been treated by PCI. Recombinant human brain natriuretic peptide (rhBNP) possesses the same amino acid sequence and mode of action with endogenous peptides-brain natriuretic peptide (BNP) secreted by ventricular myocytes. RhBNP is conductive to even blood vessels dilation, diuresis and sodium excretion, reduction of the pre-load and pro-load of heart and the correction of blood stream dynamics disorder for heart failure patients. Meanwhile, it can inhibit the activation of neuroendocrine and improve ventricle remodeling.

From February 2012 to October 2015, bioZ-2011 non-invasive hemodynamic real-time monitoring system was

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employed to monitor the hemodynamic parameters to investigate the effects of rhBNP after PCI on non-invasive hemodynamic in acute myocardial infarction patients with left ventricular failure.

2. Materials and methods

2.1. Clinical materials

A number of 96 acute myocardial infarction patients accompanied with heart failure after PCI who were hospitalized in the Department of Cardiology of the People's Hospital of Sanya during February 2012 to October 2015 were selected. Among them, 52 cases were males and 44 cases were females with ages ranging from (53.5 ± 8.4) years. The inclusion criteria include: 1. Ages between (30–75) years old without gender limitation; 2. The diagnose standard of AMI was in accordance with the clinical implications of the third universal definition of myocardial infarction [1]; 3. The indication of PCI was conducted on the basis of the internationally existed standards [2]; 4. The Killip classification of acute myocardial infarction patients with left ventricular failure after PCI was II–IV. The exclusion criteria were: 1. Patients with cardiogenic shock or a systolic pressure of ≤90 mmHg after treating with booster drugs; 2. Patients treated with monarkite or contraindicant vein vasodilator; 3. Patients accompanied with other diseases, such as malignant tumors, infectious diseases, mental disorders and so on and also patients with incomplete materials.

2.2. Treatment and monitoring methods

Those selected patients were randomly divided into the control group ($n = 46$) and the therapy group ($n = 50$). Patients in the control group were given routine antithrombotic therapy, coronary dilatation, diuresis and cardiac load reduction, ACEI or ARB, β receptor blocker, lipid regulation, plaque stabilization, etc, while patients in the therapy group, base on the routine treatment, were treated with rhBNP (trade name: Natriuretic peptide, 0.5 mg/piece) (Tibet Rhodiola Pharmaceutical Holding Co.) (1.5 μg/kg was intravenously injected with uniform speed in the first three minutes, followed by continuous infusion of 0.007 5 μg/kg·min for 72 h).

In this study, BioZ-2011 non-invasive hemodynamic monitoring instrument was used and operated in the light of the instructions carefully and faithfully to determine the hemodynamic parameters at 30 min, 1 h, 3 h, 6 h, 12 h, 24 h, 48 h, 72 h before and after treatment which included heart rate, blood pressure, stroke volume, cardiac index, peripheral vascular resistance, etc, and the plasma NT-proBNP level, renal function, electrolyte and urine volume of the two groups before and after treatment were also monitored.

2.3. Statistical methods

All data of the selected patients were collected by well-trained professional doctors before patients were grouped. The main data included non-invasive hemodynamic monitoring, blood samples, urine samples and so on. Professional statistics software SPSS21.0 was applied to deal with statistics. Measurement data of the two groups were tested by t-test. Comparison of means of more than two groups was analyzed by One-way ANOVA. Comparison of enumeration data between groups was tested by Chi-square test. Differences showed statistical significance when $P < 0.05$.

3. Results

3.1. General clinical materials

The clinical materials of those 50 and 46 cases in the two groups including gender, age, histories of hypertension, diabetes, hyperlipidemia, smoking, heart function classification and so on showed no statistical significance ($P > 0.05$), which indicated a good balance and comparability (Table 1).

3.2. Hemodynamic parameters

Data of the hemodynamic parameters at different time points of the two groups were shown in Tables 2–4.

The results showed that the heart rate (HR) of patients in the therapy group was not influenced. After treating for one hour, their blood pressure was declined; the cardiac output (CO), cardiac index (CI), stroke volume (SV) and stroke index (SI) increased obviously after treating for 0.5 h; the LVET could extended after treating for 3 h; TFC could be reduced after 6 h. However, as for the control group, the clinical effect worked relatively late, which implied that the therapy group had a faster and more effective improvement effect of hemodynamics as compared with the control group.

3.3. NT-proBNP, urine volume and renal function index

The results revealed that after treating 72 h the serum creatinine level of patients in the therapy group decreased, while their blood potassium and blood sodium showed no significant changes. In addition, their urine volume increased evidently and the NT-proBNP improved apparently. The improvement of renal function, urine volume and NT-proBNP of the therapy group was better than that of the control group (Tables 5 and 6).

Table 1
General clinical materials of patients in the two groups.

Terms	Therapy group	Control group	P
Gender (male/female)	28/22	24/22	0.710
Age (year)	66.72 ± 6.33	67.83 ± 4.90	0.340
Hypertension (n; %)	16 (32%)	20 (43%)	0.410
Hyperlipidemia case (n; %)	24 (48%)	21 (46%)	0.820
Diabetes (n; %)	16 (32%)	12 (26%)	0.530
Smoking (n; %)	12 (24%)	10 (22%)	0.790
Heart function classification			
Killip II (n; %)	13 (26%)	12 (26.1%)	0.994
Killip III (n; %)	29 (58%)	27 (58.7%)	–
Killip IV (n; %)	8 (16%)	7 (15.2%)	–

Table 2

Comparison of HR, SBP and DBP monitored at different time points of the two groups.

Time (h)	HR (time/min)		SBP (mmHg)		DBP (mmHg)	
	Therapy group	Control group	Therapy group	Control group	Therapy group	Control group
0	64.56 ± 3.73	65.98 ± 5.29	125.10 ± 21.39	129.78 ± 22.26	82.40 ± 20.91	87.87 ± 19.70
0.5	66.24 ± 4.65	67.78 ± 5.94	118.98 ± 11.88	125.41 ± 14.32	79.84 ± 13.40	80.00 ± 11.23
1	66.78 ± 5.99	68.59 ± 5.95	110.50 ± 10.70*#	125.80 ± 10.24	74.16 ± 10.25*#	81.61 ± 10.71
3	67.08 ± 4.84	68.22 ± 5.48	110.64 ± 12.32*#	120.67 ± 12.83	70.00 ± 14.31*#	80.26 ± 10.76
6	68.12 ± 5.29	69.09 ± 5.72	109.88 ± 10.88*#	118.20 ± 11.62	71.14 ± 12.21*#	79.61 ± 9.30
12	66.46 ± 4.18	67.93 ± 5.20	107.14 ± 11.15*#	117.20 ± 12.63	70.06 ± 11.90*#	75.78 ± 11.57
24	66.74 ± 4.24	68.07 ± 4.65	108.16 ± 11.17*#	120.48 ± 10.40	72.18 ± 9.04*#	75.61 ± 10.21
48	67.62 ± 3.49	68.07 ± 4.65	110.46 ± 9.69*#	121.22 ± 11.65	72.48 ± 7.64#	73.37 ± 9.49#
72	67.50 ± 3.27	67.54 ± 4.88	112.14 ± 9.12*	119.24 ± 13.03	74.80 ± 7.38#	72.11 ± 8.85#

*$P < 0.05$ compared with the control group; #$P < 0.05$ compared with level before treatment.

Table 3

Comparison of CO, CI and SV monitored at different time points of the two groups.

Time (h)	CO		CI		SV	
	Therapy group	Control group	Therapy group	Control group	Therapy group	Control group
0	4.51 ± 0.55	4.52 ± 0.52	2.44 ± 0.29	2.46 ± 0.28	58.10 ± 8.06	57.09 ± 6.59
0.5	4.74 ± 0.51*#	4.53 ± 0.51	2.62 ± 0.20*#	2.51 ± 0.28	62.78 ± 6.58*#	59.09 ± 7.42
1	4.77 ± 0.49*#	4.54 ± 0.52	2.64 ± 0.33*#	2.52 ± 0.26	63.28 ± 6.86*#	59.09 ± 7.42
3	4.80 ± 0.44*#	4.57 ± 0.50	2.69 ± 0.36*#	2.53 ± 0.25	64.04 ± 6.39*#	59.63 ± 7.58
6	4.84 ± 0.44*#	4.68 ± 0.47#	2.75 ± 0.29*#	2.55 ± 0.25	65.06 ± 5.85*#	61.07 ± 7.49#
12	4.86 ± 0.44*#	4.69 ± 0.47#	2.80 ± 0.33*#	2.60 ± 0.23#	65.98 ± 5.64*#	61.11 ± 7.48#
24	4.88 ± 0.43*#	4.70 ± 0.46#	2.85 ± 0.34*#	2.61 ± 0.23#	66.40 ± 5.36*#	62.17 ± 7.55#
48	4.87 ± 0.43*#	4.71 ± 0.48#	2.90 ± 0.35*#	2.68 ± 0.22#	67.38 ± 5.30*#	62.52 ± 6.55#
72	4.91 ± 0.43*#	4.75 ± 0.42#	2.96 ± 0.37*#	2.72 ± 0.21#	67.90 ± 5.33*#	63.63 ± 6.69#

*$P < 0.05$ compared with the control group; #$P < 0.05$ compared with level before treatment.

Table 4

Comparison of SI, LVET and TFC monitored at different time points of the two groups.

Time (h)	SI		LVET		TFC	
	Therapy group	Control group	Therapy group	Control group	Therapy group	Control group
0	33.94 ± 5.72	32.42 ± 5.96	289.52 ± 14.66	288.70 ± 14.54	28.60 ± 2.51	28.98 ± 2.52
0.5	37.74 ± 4.72*#	33.59 ± 6.07	287.80 ± 13.82	288.43 ± 13.62	28.38 ± 3.50	29.02 ± 2.66
1	38.24 ± 4.72*#	34.01 ± 5.92	287.86 ± 13.78	288.09 ± 11.62	28.16 ± 3.27	28.96 ± 2.60
6	39.32 ± 5.03*#	36.06 ± 5.90#	286.28 ± 14.18*#	288.00 ± 12.13	27.44 ± 3.30*#	28.72 ± 3.17
12	39.82 ± 4.78*#	37.39 ± 5.90#	285.80 ± 13.32*#	287.83 ± 12.25	27.38 ± 3.20*#	28.61 ± 2.82
24	40.26 ± 5.50*#	37.76 ± 5.87#	284.86 ± 12.78#	285.83 ± 12.25#	27.24 ± 3.16#	27.37 ± 3.07#
48	41.32 ± 4.63*#	38.13 ± 5.80#	284.06 ± 14.20#	284.35 ± 12.75#	26.16 ± 3.52#	27.43 ± 2.77#
72	41.82 ± 4.58*#	38.33 ± 5.80#	283.20 ± 14.44#	284.20 ± 12.52#	26.04 ± 3.21#	27.48 ± 2.54#

*$P < 0.05$ compared with the control group; #$P < 0.05$ compared with level before treatment.

Table 5

Comparison of serum creatinine, blood potassium and blood sodium of the two groups before and after treating for 72 h.

Groups	Serum creatinine (μmol/L)		Blood potassium (mmol/L)		Blood sodium (mmol/L)	
	Therapy group	Control group	Therapy group	Control group	Therapy group	Control group
Before treatment	89.56 ± 9.21	88.07 ± 11.90	4.02 ± 0.27	4.06 ± 0.31	136.57 ± 7.86	138.74 ± 7.91
After treatment	80.26 ± 7.76*#	87.70 ± 10.31	4.10 ± 0.29	4.15 ± 0.33	138.35 ± 9.22	143.57 ± 7.76

*$P < 0.05$ compared with the control group; #$P < 0.05$ compared with level before treatment.

Table 6

Comparison of urine volume and plasma NT-proBNP level of the two groups before and after treating for 72 h.

Groups	Urine volume (mL/d)		NT-proBNP (pg/mL)	
	Therapy group	Control group	Therapy group	Control group
Before treatment	1100.6 ± 80.17	1185.17 ± 64.12	4394.00 ± 861.75	4239.13 ± 893.80
After treatment	1680.80 ± 262.20*#	1290.48 ± 103.69#	782.00 ± 338.09*#	2585.87 ± 455.30#

*Compared with the control group, $P < 0.05$; #$P < 0.05$ compared with level before treatment.

4. Discussion

AMI is a common disease which harms human health badly. AMI joint with heart failure still remains to be an important cause and one of the most severe complications for patients' death. The main reason is that in the pro-AMI period the activated neuroendocrine system, including RAAS, stomodeal nervous system, netriuretic peptide system and so on, was not inhibited effectively. High level of neuroendocrine hormone made the cardiovascular system in a state of over-stress for a long time, prompted cardiac remodeling, resulted in excessive fibrosis for cardiac muscular tissues, destroyed myocardial fibers sequence, damaged the normal cardiac pacemaker conduction system, induced myocardial ischemia and abnormal heart rate, smashed the harmony of cardiac contractile function, triggered pump failure and finally increased heart events while treating AMI.

Brain natriuretic peptide is a kind of endogenous polypeptide hormones secreted by ventricular myocytes. Its secretion level is connected with the severity of the cardiac volume load and pressure load, which plays an important role in the protective compensation mechanism of circulation dynamics volume and pressure control [3]. rhBNP is a recombinant human brain natriuretie peptide compounded by DNA technology. It has the same 32 amino acid sequences with the ventricular myocytes-produced endogenous BNP and it can also imitate the effect of endogenous brain natriuretic peptide, such as natriuresis, diuresis, reduction of the activities of angiotasis, antagonism RAAS and stomodeal nervous system, correction of the hemodynamic disorder of heart failure patients, *etc*. FDA has been allowed to use in acute decompensated heart failure since 2001, which is the only approved drug used in the field of treating heart failure during the past 30 years. At present, it has been recommended by ACCF/AHA Guideline for the Management of Heart Failure, Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults and 2014 Guideline for the diagnose and treatment of heart failure in China [4–6].

rhBNP can not only improve hemodynamic disorder, natriuresis and diuresis without affecting serum potassium and creatinine, but also fight against the over-activation of the neuroendocrine system, relieve inflammatory responses, improve ventricular remodeling and protect hearts comprehensively [7]. Jing Sun *et al.* [8] stated that patients with AMI should be treated with rhBNP after PCI as soon as possible, since it can obviously inhibit the over-activation of the neuroendocrine system, alleviate the local inflammatory responses of myocardial cells, ischemia reperfusion injury and cardiac load and interdict the initiating factors of ventricular remodeling after myocardial infarction. Besides, rhBNP can inhibit the physiological action of the activity of cardiac sympathetic nerve directly by decreasing the plasma aldosterone level and the secretion of norepinephrine [9]. Michaels [10] measured the intracoronary rheography before and after using rhBNP by intracoronary Doppler. After using brain natriuretic peptide, the diameter of coronary artery expanded 15%, the coronary resistance reduced by 23%, the intracoronary blood flow volume increased by 35% and the coronary oxygen consumption reduced by 8%. rhBNP can improve the blood supply of coronary artery effectively, lighten myocardial oxygen consumption and adjust the resistance of overall circulation and coronary circulation alternatively so as to integrate the volume load and pressure load of the whole body.

The results of this study showed that the hemodynamic indexes of AMI patients accompanied with heart failure after PCI treatment in the therapy group have been improved efficaciously. Compared with the control group, the therapy group showed a faster and more effective improvement effect on hemodynamics. After those patients were treated for 0.5 h, the CO/CI and SV/SI were improved obviously as compared with those before treatment. LVET and TFC also decreased evidently, which indicated that rhBNP could improve the hemodynamics quickly for AMI patients complicated with left heart failure after PCI treatment. Meanwhile, the urine volume of patients in the therapy group increased significantly after treatment and their plasma NT-proBNP decreased obviously, but the serum potassium and blood natrium remained unaffected, which confirmed that rhBNP played a certain protective role for the renal function for patients. A meta analysis demonstrated that rhBNP has significant positive impact on the improvement of hemodynamic parameters and risks of the increases of creatinine and urea nitrogen of rhBNP have not been found yet, which is consistent with the results of this study [11].

That study result pointed out that the earlier application of rhBNP combined with non-invasive hemodynamic monitoring system can improve the hemodynamic parameters of AMI patients accompanied with heart failure after PCI without the expense of fastening heart rate and increasing cardiac work efficiency and myocardial oxygen consumption. Besides, in the treating process, side effects such as electrolyte disturbances, unstable blood pressure have not been found after the diuresis and vasodilatory effects, which indicated that the treating methods possesses excellent security and physiological tolerance and it can be widely recommended and used in clinic.

Conflict of interest statement

We declare that we have no conflict of interest.

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